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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,451	08/21/2003	Joseph L. Bryant	4115-150 CIP DIV	7909

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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EXAMINER	
NOBLE, MARCIA STEPHENS	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,451	BRYANT ET AL.	
	Examiner	Art Unit	
	Marcia S. Noble	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *12-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/21/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's election with traverse of Group I, claims 1-11 in the reply filed on 4/7/06 is acknowledged. The traversal is on the ground(s) that the inventions must be independent and distinct and both requirements have not been met and furthermore a search of all the inventions would not be a burden. This is not found persuasive because first the independent and distinct arguments is not a proper interpretation of the MPEP for restriction practice and second the additional search would be a burden to the Office.

The definition of distinct as defined by the MPEP 802.01 [R-3] is two or more inventions are related (i.e., not independent) if they are disclosed as connected in at least on of design, operation, or effect. Related inventions are distinct if the inventions as claimed are not connected in at least one design, operation, or effect and wherein at least one invention is patentable distinct over the other. "There are two criteria for a proper restriction between patentably distinct inventions:

(a) The invention must be independent (see MPEP § 802.01, § 806.06, § 808.01 or distinct as claimed (see MPEP §806.05 – 806.05(j)); and

(b) There would be a serious burden on the examiner if restriction is not required (see MPEP § 803.02, § 808, and § 808.02)."

The search of the different groups would be considered a search burden because the search strategy would be different even though they may be classified together or related in concept or subject matter. Because of the significant reliance

upon the non-patent literature in examination of the biotechnology art, applications are rarely searched by classification and are more commonly search by terminology, therefore search burden is based upon additional or different terms that must be added to the search query. In the instant case, additional terms such as lentiviral, antagonist, symptoms of HIV, treatment compounds, drugs, and inhibit HIV infection would each need to be added as individual search queries and these would each need to be search in several different databases, therefore resulting in multiple additional searches. This level of additional search is consider undue and would be considered a search burden for the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 12-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/7/06.

Claims 1-11 are under consideration.

Priority

2. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/058,113, filed 4/9/1998, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

The instant application is a divisional of 09/685,256, filed 10/10/00, which is a CIP of 09/058113, filed 4-9-1998. Application 09/685,256 discloses the invention in the specification as claim. Application 09/058113 discloses the production of an HIV/human CD4 double transgenic rat or a HIV/HIV coreceptor (CCR5 or CXCR4). Application 09/058113 does not disclose the combination of a human CD4/CCR5 transgenic rat or the human CD4/CXCR4 transgenic rat. Accordingly, the priority for the claimed subject matter is determined to be the filing date of Application 09/058113, i.e. 10/10/00.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic rat, whose genome comprises a transgene encoding a portion of or a full length CD4 protein that binds to gp120 and CCR5 or CXCR4, if present, and mediates entry of HIV and wherein the CD4 transgene contains a PMBC specific promoter resulting in expression of the CD4 on PMBCs of the transgenic rat and wherein the transgenic rat further comprises a second transgene in its genome encoding a CCR5 or CXCR4 wherein the second transgene comprises a

PMBC specific promoter resulting in the expression of CCR5 or CXCR4 on PMBCs, does not reasonably provide enablement for a transgenic rat, whose genome comprises at least one copy of a transgene encoding at least a portion of a CD4 protein sufficient for binding to gp120, wherein CD4 encoded by the transgene is expressed on PMBCs of the transgenic rat and wherein the genome further comprises a transgene encoding for at least a portion of CCR5 or a gene encoding CXCR4 . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue".

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge

pertinent to an art at the time of invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The instant specification discloses that the mechanism by which HIV-1 can infect PBMCs is via CD4 binding gp120 and also interacting with the CCR5 or CXCR4 receptor pathway on the surface of PBMCs (p. 19, lines 32-33 to p. 20, lines 1-2). Therefore it is necessary that the transgenes be targeted and expresses in a tissue specific manner, ie via a PBMC specific promoter. In the instant invention, artisan would not know how to target and promote PBMC specific expression using any other type of promoters other than a PBMC specific and result in PMBC expression and HIV infection mediated by CD4 and its interaction with gp120 and an HIV coreceptor, such as CCR5 or CXCR4. Therefore an artisan would not know how to use or make the instant invention using any other means of PMBC specific expression than with the use of a PMBC promoter.

Therefore, the invention is only enabled a transgenic rat, whose genome comprises a transgene encoding a portion of or a full length CD4 protein that binds to gp120 and CCR5 or CXCR4, if present, and mediates entry of HIV and wherein the CD4 transgene contains a PMBC specific promoter resulting in expression of the CD4 on PMBCs of the transgenic rat and wherein the transgenic rat further comprises a second transgene in its genome encoding a CCR5 or CXCR4 wherein the second transgene comprises a PMBC specific promoter resulting in the expression of CCR5 or CXCR4 on PMBCs, does not reasonably provide enablement for a transgenic rat.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites the limitation "the encoded transgene". There is insufficient antecedent basis for this limitation in the claim.

Claims 5 recites "the encoded transgene is capable of mediating entry of HIV." However, multiple transgenes are present (ie CD4 and CCR5). It is unclear if "the encoded transgene mediating entry of HIV" is meant to be CD4, CCR5, or both, therefore the claim is considered indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Goldsmith et al (US Pat # 6,372,956 B1 4/16/2002; filing date 12/23/1999).

The instant invention is drawn to a transgenic rat whose genome comprises at least a portion of or the full length human CD4, wherein the CD4 encoded by the transgene is expressed on PMBCs. The transgenic rat can further comprise a transgene encoding CCR5 or CXCR4. The instant invention also claims cells, germ cell, somatic cells, and eggs from these transgenic rats.

Goldsmith et al discloses transgenic rats that express human CD4, human CD4 and CCR5, and CD4 and CXCR4 on lymphocytes. CD4/CCR5 mice were produced by crossing CD4 and CCR5 transgenic mice (Example 5 and 6, col 20). Goldsmith et al disclose that the human CD4 can be a partial sequence or a full lengh sequence that is encoded (col 9, lines 51-53). They also disclose the double transgenic can be produced with CCR5 or CXCR4 and provide disclosure of sequences that can be used (col 11, line 53 and col 12 Table 1 and 2). They also disclose that splenocytes from CD4/CCR5 transgenic rats were infected by HIV-1 strains (col 21lines 10-11).

Because the transgenic rat is disclosed by Goldsmith et al, cells, germs cells, somatic cells and eggs from the transgenic rat are inherent to the disclosure of the transgenic rat. In other words, if an artisan has the rat, they have and can obtain cells from said rat by methods well established in the art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Browning et al (PNAS 94:14637-14641, 1997).

The instant invention is drawn to a transgenic rat whose genome comprises at least a portion of or the full length human CD4, wherein the CD4 encoded by the transgene is expressed on PMBCs. The transgenic rat can further comprise a transgene encoding CCR5. The instant invention also claims cells, germ cell, somatic cells, and eggs from these transgenic rats.

Browning et al teaches a bi-transgenic mouse expressing human CD4 and CCR5 that are expressed on lymphocytes and are infected by HIV1 (see abstract, whole document, fig 5). Browing et al does not teach a transgenic rat.

It would be obvious to an artisan to produce a CD4/CCR5 transgenic rat with a reasonable expectation of success because the methods of producing transgenic mice and rats were developed at the same time, have the same efficiency, can utilized the

same vectors, and have often been used interchangeably. The species is not the novelty of the invention, it is the expression of the transgene in a rodent model.

Because the transgenic rat is taught by Browning et al, cells, germs cells, somatic cells and eggs from the transgenic rat are inherent to the disclosure of the transgenic rat. In other words, if an artisan has the rat, they have and can obtain cells from said rat by methods well established in the art.

8. Claims 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sawada et al (J Exp Med 187(9):1439-1449).

The instant invention is drawn to a transgenic rat whose genome comprises at least a portion of or the full length human CD4, wherein the CD4 encoded by the transgene is expressed on PMBCs, and comprise a gene encoding CXCR4.

Sawada et al teach the production of transgenic mice that express CD4 and CXCR4 on lymphocytes (see abstract and p. 1140 col1 par 2).

It would be obvious to an artisan to produce a CD4/CCR5 transgenic rat with a reasonable expectation of success because the methods of producing transgenic mice and rats were developed at the same time, have the same efficiency, can utilized the same vectors, and have often been used interchangeably. The species is not the novelty of the invention, it is the expression of the transgene in a rodent model.

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcia S. Noble whose telephone number is (571) 272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marcia S. Noble